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Transgender People and HIV Prevention: What We Know and What We Need to Know, a Call to Action

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Abstract: Transgender people have been disproportionately affected by HIV, particularly transgender women. Their increased vulnerability to HIV is due to multiple issues, including biological (eg, increased efficiency of HIV transmission through receptive anal sex), epidemiological (eg, increased likelihood of having HIV-infected partners), structural (eg, social stigma limiting employment options), and individual factors (eg, internalized stigma leading to depression and substance use and risk-taking behaviors). There have been limited culturally appropriate HIV prevention interventions for transgender people, with many key prevention studies (eg, the iPrEx PrEP study) enrolling transgender women in a study focusing on men who have sex with men. This has resulted in limited understanding of the optimal ways to decrease transgender people's risk for HIV acquisition. The current supplement of *JAIDS* is designed to review what is known about HIV prevention for transgender people and to highlight new insights and best practices. The study reviews recent epidemiologic data, the pharmacology of HIV prophylactic agents in individuals who may be using exogenous hormones, and several recent multi-component interventions designed to address the lived experience of transgender people. Additionally, the study reviews the work going on at the NIH to address transgender health in general and HIV prevention in specific, as well as two important papers related to clinical trial design issues and the ethical conduct of research in this frequently disenfranchised population. It is the hope of the HIV Prevention Trials Network (HPTN) that this supplement will promote new knowledge around transgender health and the requisite issues that need to be addressed in order to conduct optimal clinical trials. The ultimate hope is that the information distilled in this supplement will inform investigators, clinicians, and public health officials in order to design further research to develop optimal prevention interventions for transgender

people and to implement these interventions in ways that are culturally congruent and health promoting.

Key Words: HIV prevention, transgender, HIV/AIDS

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Since the earliest days of the AIDS epidemic, it has been recognized that transgender women have had disproportionate rates of HIV infections and AIDS-related mortality.¹ Transgender women and men constitute less than 1 percent of the general population in the US, but in many epidemiologic studies, HIV prevalence has been in the double digits for transgender women, with wide variations depending on how the population was recruited.^{2,3} Much less is known about transgender men and HIV, but several studies have documented that a significant number may identify as “gay,” and/or engage in sexual and drug-using behaviors that increase their risk for HIV acquisition.^{4,5} Thus, one of the early challenges to adequately understand the dynamics of HIV transmission for transgender people has been their relatively low representation in the general population, but distinctively increased burden of HIV disease.

Individual factors that potentiate the HIV epidemic in transgender women include engaging in receptive anal intercourse⁶ and a high likelihood of having partners who may be at increased risk for HIV.⁷ Internalized transphobic stigma may result in depression and substance use, which also potentiate HIV risk taking.^{8–10} For many years, epidemiologic studies did not distinguish transgender women from cisgender men who have sex with men in the composite acronym “MSM,” because they were perceived to have common risk for HIV acquisition through anal sex, complicating optimal understanding of the epidemiology of HIV among transgender individuals, and their specific HIV prevention needs. This has been a disservice to transgender women, in particular, because the social and structural factors that increase the susceptibility of transgender women to HIV differ substantially from those of cisgender men who have sex with men. For example, in many cultures, transgender individuals are recognized as having a distinct gender minority status, eg, hijra in India and katoiy in Thailand, as well as 2-spirit individuals in Native American populations^{11–13} However, this recognition as a distinct social grouping has also been associated with unique manifestations of stigma, including challenges to maintaining an adequate livelihood, resulting in poverty.¹⁴ Thus in many settings, transgender individuals have been forced to rely on sex work to survive, further exacerbating their risk for HIV.⁷ In

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addition, the category “MSM” has often not included transgender men who have sex with men, stymying knowledge of HIV risks in this potentially at-risk group.

To address the conundrum of developing culturally tailored programs that are effective in decreasing HIV incidence for transgender individuals, the first fundamental is having an appropriate understanding of the epidemiology of behaviors and risks with specific types of partners in the diverse cultures where transgender people live. However, the social convention of referring to “transgender people” is problematic since identity, behavior, and risk do not necessarily map in a uniform manner. For example, epidemiologic studies suggest that some transgender women are at particularly high risk for HIV because of anal intercourse and sex work.^{2,11,14} But, many of the studies to date that inform these presumptions have recruited potential participants for the purpose of HIV prevention research, which could lead to inherent biases due to sampling (ie, only recruiting in risky venues). For transgender men, the literature is limited with some studies suggesting lower HIV risks, whereas other studies have suggested elevated risk compared with cisgender men in the same communities.^{4,15} Some transgender men who are assigned a female sex at birth may subsequently identify as “gay” and therefore also engage in anal intercourse, as well as frontal/vaginal intercourse if preoperative, and be at risk for HIV.^{4,8,15,16} It is extremely important that in the design of prevention programs or research for transgender people, there is an appreciation of the heterogeneity of transgender people, and that interventions are culturally tailored to the needs of specific communities.

Over the past decade, there has been an increased awareness that the appropriate use of antiretroviral drugs can be highly effective in decreasing HIV transmission globally.¹⁷ Early initiation of antiretroviral therapy is not only beneficial to the health of people living with HIV but can significantly reduce the risk of HIV transmission.¹⁸ Multiple studies have also indicated that the use of pre-exposure prophylaxis (PrEP) by HIV-uninfected individuals can significantly decrease HIV acquisition.¹⁹ However, to date, the benefits of these important prevention approaches have not been manifested among transgender women and men in many parts of the world. Because of high levels of social stigma and often structural violence, transgender people have not been able to avail themselves of available testing, prevention, care, and treatment services.^{20,21} In addition, the use of PrEP presumes that individuals are comfortable with discussing their sexual behaviors with health providers, in settings where health care system transphobia is common.^{22,23} The only PrEP study that recruited a sufficient number of transgender women was the iPrEx study, in which there was no benefit found for transgender women using prophylactic medication, likely due to small number of such participants.²⁴ But, through careful analysis of the 21 transgender women who became HIV-infected among those who participated in iPrEx, it was evident that these transgender women were not adherent to study medication because none of them had detectable drug in the blood at the time of infection.²⁵

Future PrEP and treatment as prevention studies for transgender women should address the factors that may lead to suboptimal adherence in this population, including, where

possible, the need to provide comprehensive medical and primary care services that integrate hormonal and surgical care with antiretroviral management, and address individual issues, such as depression, substance use, economic, and housing instability, and the structural drivers of these syndemic conditions. Where “one-stop” care is not feasible, it is incumbent on local clinicians and programs to identify appropriate referrals and to optimize the local standard of care. Questions remain as to whether the supraphysiologic doses of hormones that transgender people may use to medically affirm their sex could be interacting with antiretroviral medication and attenuating the benefits of PrEP.^{26–28} There are no data at present to suggest that high doses of feminizing or masculinizing hormones would negate the benefit of daily oral tenofovir and emtricitabine for PrEP, but this area has not been sufficiently studied and new work is underway to fully address the issue of whether hormonal medication could interact with medications used for PrEP. In addition, it is critical that every effort be made to establish comprehensive services that meet the unique needs of this population, including availability of responsive and sensitive providers. Involvement of transgender individuals in the design of such services and research efforts is fundamental to their success.

This Journal supplement has been developed to provide information on the state of the HIV epidemic among transgender individuals and to inform the way forward in responding to this public health challenge. The supplement builds on a workshop sponsored by the HIV Prevention Trials Network in June, 2015. In the first article, **Dr. Tonia Poteat** et al²⁹ review the global epidemiology of HIV and syndemic conditions among transgender individuals. **Dr. Peter Anderson** et al³⁰ discuss available information about the interaction between exogenous hormones and antiretroviral drugs. The article contributed by **Dr. Robert Grant** et al³¹ delineates what has been learned from the iPrEx study about transgender women’s participation in one of the first PrEP studies and discusses new directions for further research in this area. **Dr. Sari Reisner** et al³² discuss a holistic framework for understanding the optimal health needs of transgender people so that they can avoid HIV acquisition, and that if they become infected, how they can live healthy and productive lives. **Dr. Robert Garofalo** et al³³ discuss behavioral interventions that are evidence based and are socially congruent for transgender women to optimize HIV protection. **Dr. Rona Siskind** et al,³⁴ who coordinated a trans-NIH working group on sexual and gender minority issues, discuss the efforts underway at the NIH to ensure that ongoing and future clinical trials are sensitive to the realities of the people being studied. **Dr. Jim Hughes** et al³⁵ discusses statistical considerations in the evaluation of HIV prevention interventions in populations that are not highly represented in the general population but whose risk for HIV acquisition and transmission is high. Last but not certainly not least, **Dr. Jerome Singh** et al³⁶ discusses the ethical considerations for conducting research among transgender individuals given frequently coprevalent societal stigma and structural violence.

The intent of this supplement is to frame the issues of importance in developing a more holistic approach to the

development of HIV prevention interventions for transgender individuals. To conduct optimal research, many of the underlying social and structural issues need to be addressed. Transgender individuals need to achieve civic equality in all societies so that they will be comfortable disclosing their status and participating in research in an environment that they feel is just and beneficent. Their involvement in the design of research studies and programs is fundamental. In addition, resources need to be available to allow transgender individuals to achieve their full potential and not to have to rely on transactional behaviors for survival in an adversarial environment. Thus, although this special issue is focused on issues that may inform the conduct of future research, it is also a clarion call for social justice for transgender individuals so they can be fully empowered members of their societies and avail themselves of the benefits of the new advances in HIV prevention and care.

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